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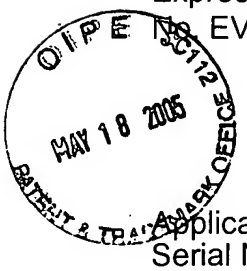

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Robert A. Holton
Serial No. 10/606,027
Filed June 25, 2003
Confirmation No. 3976
For C7 ESTER SUBSTITUTED TAXANES
Examiner Ba K. Trinh

Art Unit 1626

May 18, 2005

NOTICE OF FILING BRIEF ON APPEAL FROM THE EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

TO THE COMMISSIONER FOR PATENTS,

SIR:

* Appellant hereby files its Brief on Appeal to the Board of Patent Appeals and Interferences. This appeal is from the Examiner's decision mailed July 28, 2004, finally rejecting the claims. A Notice of Appeal was mailed January 19, 2005.

* The brief fee of $500.00 is enclosed. If there are any additional charges in this matter, please charge our Deposit Account No. 19-1345.

Respectfully submitted,

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BRIEF FOR APPELLANTS

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Robert A. Holton
Serial No. 09/776,492
Filed February 2, 2001
Confirmation No. 2712
For C10 ESTER SUBSTITUTED TAXANES
Examiner Ba K. Trinh

Art Unit 1625

BRIEF FOR APPELLANTS

This is an appeal from the final rejection of the above-identified application made in the Office action mailed July 28, 2004. A Notice of Appeal was mailed on January 19, 2005.

I. REAL PARTY IN INTEREST

The real party in interest is Florida State University, owner of a 100 percent interest in the pending application.

II. RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any pending appeals or interferences which may directly affect or be directly affected by, or have a bearing on, the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 1-85, 89-95, 102-108, 115-117, 122-132, 134-137, 140-146, 148-150, 153-159, 161-163 and 166-169 are pending in this application. The claims on appeal are set forth in full in the Appendix to this Brief.

Claims 1-85, 89-95, 102-108, 115-117, 122-132, 134-137, 140-146, 148-150, 153-159, 161-163 and 166-169 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of Holton et al., U.S. Patent No. 6,642,208.

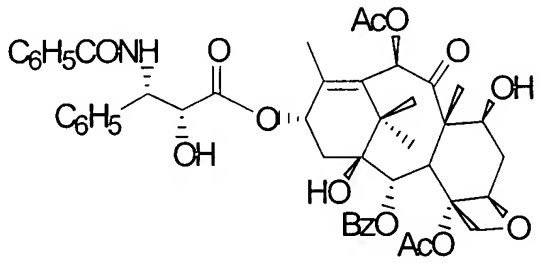
IV. STATUS OF AMENDMENTS

The amendments filed subsequently to the final rejection were entered.

V. SUMMARY OF THE INVENTION

The present invention is directed to novel taxanes which have exceptional utility as anti-tumor agents. In particular, the present invention is directed to taxanes which compare favorably to taxol (paclitaxel) and docetaxel with respect to efficacy as anti-tumor agents and with respect to toxicity.[1] In general, these taxanes possess an ester substituent other than formate, acetate and heterosubstituted acetate at C-7, a hydroxy substituent at C-10 and a limited range of C-3' substituents.

The taxane family of terpenes, of which baccatin III and taxol (paclitaxel) are members, has been the subject of considerable interest in both the biological and chemical arts. Taxol is employed as a cancer chemotherapeutic agent and possesses a broad range of tumor-inhibiting activity. Taxol has a 2′R, 3′S configuration and the following structural formula:



wherein Ac is acetyl.[2]

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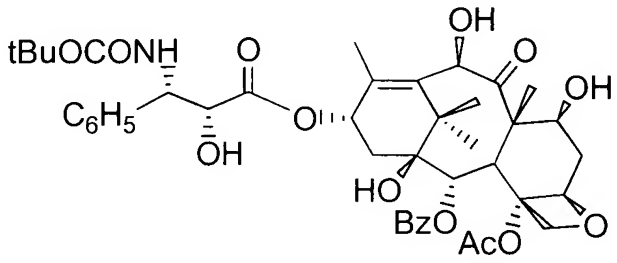
[1]Specification, page 2, lines 6-9.

[2]Specification, page 1, lines 11-14.

Colin et al. reported in U.S. Patent 4,814,470 that certain taxol analogs have an activity significantly greater than that of taxol. One of these analogs, commonly referred to as docetaxel, has the following structural formula:[3]



Although taxol (paclitaxel) and docetaxel are useful chemotherapeutic agents, there are limitations on their effectiveness, including limited efficacy against certain types of cancers and toxicity to subjects when administered at various doses. Accordingly, a need remains for additional chemotherapeutic agents with improved efficacy and less toxicity.[4]

VI. ISSUE

The only issue presented on appeal is whether claims 1-85, 89-95, 102-108, 115-117, 122-132, 134-137, 140-146, 148-150, 153-159, 161-163 and 166-169 are unpatentable based on the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of Holton et al., U.S. Patent No. 6,642,208 (hereinafter referred to as the "'208 patent").

VII. GROUPING OF CLAIMS

For purposes of this appeal, claims 1-85, 89-95, 102-108, 115-117, 122-132, 134-137, 140-146, 148-150, 153-159, 161-163 and 166-169 do not stand or fall together. The claims have been divided into six groups: Group I (claims 1, 122-125,

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[3]Specification, page 1, lines 16-19.

[4]Specification, page 1, line 20 - page 2, line 2.

140-142 and 153-155), Group II (claims 2-29), Group III (claims 30-57, 126-129, 143-145 and 156-159), Group IV (claims 58-85, 130-132, 135-137, 146, 148-150, 159 and 161-163), Group V (claims 89-95 and 166-169) and Group VI (claims 102-108 and 115-117). The claims of each of Group I - Group VI are separately and independently patentable for the reasons described in Sections VIII(B)(1) through VIII(B)(6), *infra*.

VIII. ARGUMENT

A. The Office's Reliance Upon Reaction Scheme 12 of the '208 patent is Improper

An obviousness-type double patenting rejection is appropriate only when the claims of an application would have been obvious to one of ordinary skill in the art from the claims of an issued patent upon which the double patenting rejection is based. The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. 103 obviousness determination.[5] An important distinction, however, exists. A rejection for obviousness must be based on a comparison of the invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the invention to the claims, **and only the claims**, of the reference.[6]

In the Office action dated July 28, 2004, the Office cited Reaction Scheme 12 of the '208 patent in support of the obviousness-type double patenting rejection[7] and in the telephonic interview of record, the Examiner relied on Example 1 to support the rejection. However, such reliance is improper. Even though the '208 patent specification may be considered a § 102 (b) reference, as recognized by applicant in

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[5]In re Braat, 937 F.2d 589 (Fed. Cir. 1991).

[6]Purdue Pharma L.P. v. Boehringer Ingelheim GMbH, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).

[7]See Office action dated July 28, 2004, page 2.

the reply to the Office action dated July 28, 2004, there has been no statutory rejection of the pending claims. An obviousness-type double patenting rejection must be grounded on a comparison of the invention to the claims, **and only the claims**, of the applied reference.

B. The Office has Failed to Establish a *Prima facie* Case that Claims 1-85, 89-95, 102-108, 115-117, 122-132, 134-137, 140-146, 148-150, 153-159, 161-163 and 166-169 are Obvious in Light of the '208 Patent Claims

According to the Office, the claims of the present application and claims 1-9 of the '208 patent are

> not patentably distinct from each other because the R_7 group of the patented compound is an acyl group wherein the acyl contains methyl, ethyl and the like which read on the current R_7 group; i.e., hydrocarbyl.[8]

The Examiner's analysis hinges on this statement, which is replete with error.

Novelty and obviousness must be evaluated in consideration of the claimed invention as a whole.[9] Here the claimed compound differs from claims 8 and 9 of '208 with regard to multiple substituents at multiple different positions. Indeed, the substituents which differ include R_7. But even if claim 1 did not distinguish claim 8 and 9 at the C7 position, claim 1 would remain novel and nonobvious based on differences in substituents at multiple other positions, i.e., C1, C4, C5, C8, C2' and C3'N.

Moreover, even as to R_7, the Examiner has unfortunately applied the novelty test backwards, and thereby reached a clearly erroneous result. The question is not whether R_7 of claims 8 and 9 reads on R_7 of claim 1, but instead whether R_7 of claim 1 reads on claims 8 or 9. Manifestly, it does not. Whereas R_7 of '208 patent claims 8 and 9 calls generically for "acyloxy," R_7 of instant claim 1 is limited to substituents in which

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[8]Office action mailed July 28, 2004, page 2.

[9]In re Kuderna, 165 U.S.P.Q. 575 (C.C.P.A. 1970), Jones v. Hardy, 727 F.2d 1524, 220 USPQ 1021 (Fed. Cir. 1984).

the "hydrocarbyl" constituting R_{7a} comprises a carbon atom both alpha and beta to the carbonyl group that attaches to the ring through an oxygen. This definition is distinctly narrower than acyloxy, both in limiting R_{7a} to "hydrocarbyl" and in specifying a minimum number of carbon atoms in the hydrocarbyl group. In order to make out a *prima facie* case of obviousness under 35 U.S.C. § 103, the Office must:

A. determine the scope and contents of the prior art;
B. ascertain the differences between the prior art and the claims in issue;
C. determine the level of skill in the pertinent art; and
D. evaluate any evidence of secondary considerations.[10]

Additionally, to establish a *prima facie* case of obviousness, the Office must find some motivation or suggestion to make the claimed invention in light of the prior art teachings.[11] In this case, no prior art is relied on, but obviousness is instead evaluated against the claims of the '208 patent, which fill the role that would be played by the prior art in a statutory § 103 analysis. But the necessity of motivation or suggestion to modify the claimed subject matter of the '208 patent must still be shown if the compounds claimed herein are to be found obvious. Here, a *prima facie* case of obviousness has not been established because the Office improperly defined the subject matter against which obviousness is to be evaluated and failed to make any showing of the motivation or suggestion to select the claimed species from the disclosed prior art genus.

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[10]Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966).

[11]See, e.g., In re Brower, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996).

1. The Group I Claims (Claims 1, 122-125, 140-142 and 153-155)

When evaluating the scope of a claim, every element of the claim must be considered.[12] The claimed invention may not be dissected into discrete elements to be analyzed in isolation, but must be considered as a whole.[13] Thus, while the Office has chosen to focus on the R_7 group of the claimed compounds, the entire compound, with all of its elements, must be examined.

Claim 1 is representative of the Group I claims of the present application. The following Table 1 details selected substituents of the tetracyclic taxane for subject claim 1 and compares them to the substituents cited in claims 8 and 9 of the '208 patent.

Table 1.

Substituent Position	Subject Claim 1	Claims 8 and 9 of '208
C1	β-OH	hydrogen, hydroxy, protected hydroxy, or together with R_{14} forms a carbonate
C4 and C5	β-oriented oxetane ring with an α-acetoxy substituent attached to C4	oxetane ring with an acetoxy substituent attached to C4

[12]See, e.g., In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995).

[13]See, e.g., W.L. Gore & Assoc., Inc. v. Garlock, Inc., 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

C7	$R_{7a}COO$- (R_{7a} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo wherein said hydrocarbyl or substituted hydrocarbyl contains carbon atoms in the alpha and beta positions relative to the carbon atom of which R_{7a} is a substituent)	acyloxy
C8	β-methyl	methyl
C9	keto (oxo), hydroxy or acyloxy	oxo
C10	hydroxy	hydroxy
C2'	α-OH	-OX_6 (wherein X_6 is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, hydroxy protecting group, or functional group which increases the water solubility of the taxane derivative)

C3'N	$-COX_{10}$ (wherein X_{10} is alkyl, alkenyl, alkynyl or heterocyclo) or X_5 is $-COOX_{10}$ (wherein X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, –butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, alkenyl, alkynyl or heterocyclo)	t-butoxycarbonyl
C3'	heterocyclo	furyl or thienyl

Notably, with respect to the nitrogen substitution, the compounds of claims 8 and 9 of the '208 patent and the compounds of the subject claims (particularly claims 1 and 89) are mutually exclusive (X_5 for the subject claims excludes t-butoxycarbonyl). Consequently, not only do the '208 patent claims fail to provide motivation for modifying the compounds disclosed therein to arrive at the combination of taxane substituents defined in subject claim 1, but the '208 patent claims effectively teach away from the compounds defined by claim 1.

As illustrated in the table, subject claim 1 defines compounds wherein the combination of substituent selections is different at multiple designated positions of the tetracyclic taxane structure from the compounds defined by claims 8 and 9 of the '208 patent. For example, at the C1 and C2' positions, subject claim 1 defines stereochemistry as well as a subset of the possible substituents defined in claims 8 and 9; and at the C4 and C5, and C8 positions, subject claim 1 defines stereochemistry,

whereas claims 8 and 9 do not. The Office has offered no reference, evidence or reasoning which would have led one skilled in the art to the selections and alterations of multiple substituents necessary to transform the universe of taxanes as defined in claims 8 and 9 of the '208 patent to the distinctly different compounds of claim 1 herein.

When determining whether a particular genus or species is obvious in view of the prior art, the authorities direct a consideration of "the total circumstances involved."[14] For example, where the nucleus is unchanging and only a handful of alternative substituents is permitted at each of one, two or maybe even three, positions on a reference structure, the total number of combinations and permutations may be small. In such case, it may be well within the skill of the art to draw each structure encompassed by the reference and write its chemical name, thus effectively rendering all such structures obvious. In the instant situation, by contrast, although pending claim 1 may be broader than claims 8 and 9 at some positions, the definitions of substituents in the '208 claims is broader than pending claim 1 at five different positions, i.e., C1, C4/C5, C7, C8 and C2', while the respective definitions are mutually exclusive at another, i.e., C3'N. Moreover, the total number of compounds within the purview of '208 claims 8 and 9 is vast, and essentially uncountable. While these claims specify an unchanging nucleus, it is certainly beyond the capacity of those skilled in the art to draw the structure of each compound encompassed by either claim 8 or claim 9.

A closer look at the aforesaid positions will graphically illustrate the non-obviousness of claim 1. For example, at the C1 position (e.g., R_1), considering stereochemistry and the many potential hydroxy protecting groups, there is an approximately 50-fold greater substituent variation at the C1 position in claims 8 and 9 than in instant claim 1. Similarly, for the C4 and C5 positions there is approximately a 2-fold greater substituent variation; for the C8 position, there is approximately a 2-fold greater substituent variation; and for the C2' position, there is an approximately 280-fold greater substituent variation. The substituent variation over these four positions is

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[14] In re Petering, 133 U.S.P.Q. 275, 280 (C.C.P.A. 1962).

56,000-fold greater for the compound defined by claims 8 and 9 of the '208 patent compared to the compounds defined by instant claim 1.

Moreover, the species encompassed by the C7 substituent of claim 8 and 9 is essentially unlimited. While the scope of R_7 of instant claim 1 is also substantial, the requirement of carbon atoms in both the alpha and beta positions relative to the carbonyl clearly excludes many species that fall within the purview of R_7 as defined in claim 8 and 9. Accordingly, the species covered by claims 8 and 9 but not by claim 1 at the C1, C4/C5, C8, C2' and C7 positions is clearly far greater than the 56,000-fold factor roughly estimated above.

As explained by the court in In re Ruschig,[15] the Petering opinion did not allow the "mechanistic dissection and recombination of the components of the specific illustrative compounds" of a reference to create the compounds disclosed by the applicant.[16] While there are substituent positions defined in claim 1 having greater substituent variation than those same positions defined in claims 8 and 9, the pattern of possible substituent variations is not similar between the two sets of claims. Thus, the compounds of instant claim 1 are not obvious from the claims of the '208 patent because the only way to arrive at the compounds of claim 1 from the compounds of claims 8 and 9 is by a mechanistic dissection and recombination of components that is not allowed.

Given the multiple positions at which the compounds of claims 8 and 9 of the '208 patent must be modified to transform them to the compounds defined in instant claim 1, it is apparent that such transformation can be accomplished only by a liberal application of hindsight, using Applicants' invention as a template. It is well established that hindsight is not a proper criterion.[17] The Federal Circuit has expressly warned

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[15]In re Ruschig, 145 U.S.P.Q. 274, 282 (C.C.P.A. 1965).

[16]See id.

[17]U.S. v. Adams, 383 U.S. 39 (1965).

against the natural inclination to apply an inventor's own teachings against him in evaluating obviousness.[18]

The M.P.E.P. also warns against hindsight:

> It is difficult but necessary that the decisionmaker forget what he or she has been taught ... about the claimed invention and cast the mind back to the time the invention was made ... to occupy the mind of one skilled in the art who is presented only with the references and who is normally guided by the then-accepted wisdom in the art.[19]

Furthermore, as stated above, the '208 claims teach away from the selection of the compounds of instant claim 1. The M.P.E.P. states

> [A] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.[20]

In this case, due to the obviousness-type double patenting rejection, the reference as a whole is restricted to the claims of the '208 patent. As one example, because claims 6 to 17 of the '208 patent require a t-butoxycarbonyl group at the C3'N position (e.g., X_5), these claims would have led a person of ordinary skill to the selection of a t-butoxycarbonyl at the C3'N position. In contrast, instant claim 1 does not allow a t-butoxycarbonyl group at the C3'N position. Accordingly, claims 6 to 17 of the '208 patent would have led a person of ordinary skill away from the compounds of claim 1.

As another example of teaching away from the selection of the compounds of claim 1, claims 10 to 17 of the '208 patent require a hydrogen atom at the C7 position (e.g., R_7). In other words, the claims of the '208 patent select either an unlimited acyloxy group or a hydrogen at the C7 position (e.g., R_7). As a result, a person of

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[18]Panduit Corp. v. Dennison Mfg. Co., 774 F.2d 1082, 227 USPQ 337 (Fed. Cir. 1985), vacated and remanded on other grounds, 475 U.S. 809, 106 S.Ct. 1578 (1986), adhered to on remand, 810 F.2d 1561, 1 USPQ2d 1593 (Fed. Cir. 1987).

[19]M.P.E.P. § 2141; W.L. Gore & Assoc., Inc. v. Garlock, Inc., 721 F.2d 1540, 220 U.S.P.Q. 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

[20]M.P.E.P. § 2141.02; W.L. Gore & Assoc., Inc. v. Garlock, Inc., 721 F.2d 1540, 220 U.S.P.Q. 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

ordinary skill would have been led away from selection of a particular acyloxy group and led to the selection of a hydrogen atom at the C7 position by the claims of the '208 patent. But, instant claim 1 defines particular acyloxy groups in which the "hydrocarbyl" constituting R_{7a} comprises a carbon atom both alpha and beta to the carbonyl group that attaches to the ring through an oxygen.

Claims 122-125 and 140-142 define pharmaceutical compositions of the compounds of claim 1 and are submitted to be patentable for the same reasons as claim 1. Furthermore, claims 153-155 define methods for inhibiting tumor growth by oral administration of the compounds of claim 1 and are submitted to be patentable for the same reasons as claim 1.

In summary, the Office has failed to identify any suggestion or motivation that would have led a person of ordinary skill from the compounds defined by the claims of the '208 patent to the compounds defined by the Group I claims. Accordingly, a *prima facie* case of obviousness has not been established with respect to the Group I claims.

2. *The Group II Claims (Claims 2-29)*

Claim 2 is representative of the Group II claims. It is dependent upon claim 1 and is patentable for the same reasons as those stated with respect to claim 1. It is separately and independently patentable over the claims of the '208 patent for the following reasons.

Claim 2 requires the C7 substituent (R_7) to be $-OC(O)R_{7a}$ wherein R_{7a} is C_2-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl. The compounds of claims 8 and 9 of the '208 patent have an acyloxy group at the C7 position and neither claims 8 nor 9 would have suggested the particular selection of an ester group substituted with C_2-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl group at the C7 position from the unlimited universe of acyloxy groups encompassed by the C7 substituent in claims 8 and 9. Much less do these claims suggest the entire combination of substituents to which instant claim 2 is directed. In addition, the claims of the '208 patent as a whole teach away from the

selection of compounds having the combination of various substituents defined in claim 2 and a C7 acyloxy group substituted with a C_2-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl group. The claims of the '208 patent would have led a skilled artisan not only to multiply different combinations of substituents at positions other than C7, but would also have led to selection of hydrogen at the C7 position. Accordingly, a *prima facie* case of obviousness has not been established with respect to the Group II claims.

3. The Group III Claims (Claims 30-57, 126-129, 143-145 and 156-158)

Claim 30 is representative of the Group III claims. It is dependent upon claim 1 and is patentable for the same reasons as those stated with respect to claim 1. It is separately and independently patentable over the claims of the '208 patent for the following reasons.

Claim 30 further requires R_7 to be $-OC(O)R_{7a}$ wherein R_{7a} is C_2-C_8 alkyl. Although the compounds claimed in the '208 patent have an acyloxy group at the C7 position, the multiply different combination of substituents at the other positions defined by claims 8 and 9 would not have suggested the selection of the combination of substituents at the multiple designated positions of the tetracyclic taxane and an ester group substituted with an C_2-C_8 alkyl group at the C7 position. Moreover, as described above the claims of the '208 patent as a whole would have taught away from such a combination as defined by claim 30.

Furthermore, claims 126-129 and 143-145 define pharmaceutical compositions wherein the $-OC(O)R_{7a}$ group defines R_{7a} as ethyl and propyl and claims 156-158 define methods for inhibiting tumor growth by oral administration of compounds wherein the $-OC(O)R_{7a}$ group defines R_{7a} as ethyl and propyl. As there would have been no motivation to select the particular C7 ester groups of the compounds of Group III combined with the many other taxane substituents as described above, the compounds of claim Group III are patentable in view of the claims of the '208 patent. Accordingly, a

prima facie case of obviousness has not been established with respect to the Group III claims.

4. The Group IV Claims (Claims 58-85, 130-132, 135-137, 146, 148-150, 159 and 161-163)

Claim 58 is representative of the Group IV claims. It is dependent upon claim 1 and is patentable for the same reasons as those stated with respect to claim 1. It is separately and independently patentable over the claims of the '208 patent for the following reasons.

Claim 58 further requires a propionyloxy group at the C7 position. The compounds of claims 8 and 9 differ from claim 58 at multiple positions of the taxane molecule, including *inter alia* at the C-7 position wherein claims 8 and 9 call very broadly for "acyloxy." Accordingly, the claims of '208 fail to suggest even the particular selection of propionyloxy at C-7 from the unlimited universe of "acyloxy," much less the overall combination of substituents of claim 58.

Additionally, claims 130-132, 135-137, 146 and 148-150 are directed to pharmaceutical compositions containing compounds having a propionyloxy group at the C7 position. Furthermore, claims 159 and 161-163 are directed to methods of inhibiting tumor growth by oral administration of a pharmaceutical composition containing a taxane having a propionyloxy group at the C7 position. Because the '208 patent claims would have failed to motivate selection of the multiply different combination of taxane substituents with a C7 propionyloxy group, the compounds of claim Group IV are patentable in view of the '208 patent claims. Accordingly, a *prima facie* case of obviousness has not been established with respect to the Group IV claims.

5. The Group V Claims (Claims 89-95 and 166-169)

Claim 89 is representative of the Group V claims of the present application. The following Table 2 details the substituents of the tetracyclic taxane for subject claim 89 and compares them to the substituents cited in claims 8 and 9 of the '208 patent.

Table 2.

Substituent Position	Subject Claim 89	Claims 8 and 9 of '208
C1	β-OH	hydrogen, hydroxy, protected hydroxy, or together with R_{14} forms a carbonate
C2	α-benzoyloxy	benzoyloxy
C4 and C5	β-oriented oxetane ring with an α-acetoxy substituent attached to C4	oxetane ring with an acetoxy substituent attached to C4
C7	β-R_{7a}COO- (R_{7a} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo wherein said hydrocarbyl or substituted hydrocarbyl contains carbon atoms in the alpha and beta positions relative to the carbon atom of which R_{7a} is a substituent)	acyloxy
C8	β-methyl	methyl
C9	keto (oxo)	oxo
C10	β-OH	hydroxy

C2'	α-OH	$-OX_6$ (wherein X_6 is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, hydroxy protecting group, or functional group which increases the water solubility of the taxane derivative)
C3'N	$-COX_{10}$ (wherein X_{10} is alkyl, alkenyl, alkynyl or heterocyclo) or X_5 is $-COOX_{10}$ (wherein X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, alkenyl, alkynyl or heterocyclo)	t-butoxycarbonyl
C3'	heterocyclo	furyl or thienyl

Notably, as described in detail above for Group I, the compounds of claim 89 are mutually exclusive of the compounds defined in claims 8 and 9 of the '208 patent. Moreover, the selection of the multiply different combination of substituents defined by claim 89 would not have been suggested by the claims of the '208 patent. In actuality,

as described for claim 1, the '208 patent claims teach away from the selection of the combination of substituents required by claim 89.

As described above for Group 1 for determination of obviousness, the authorities direct a consideration of "the total circumstances involved."[21] For specific substituents, for example, there is a great difference in the number of substituent variations defined by instant claim 89 and by claims 8 and 9 of the '208 patent. For the C1 position (e.g., R_1), the substituent variation defined by claims 8 and 9 is approximately 50-fold greater than for claim 89; for the C4 and C5 positions there is approximately a 2-fold greater substituent variation; for the C8 position, there is approximately a 2-fold greater substituent variation; for the C10 position, there is approximately a 2-fold greater substituent variation; and for the C2' position, there is an approximately 280-fold greater substituent variation. For the C1, C4, C5, C8, C10, and C2' substituent positions, there is an approximate 112,000-fold greater substituent variation defined by claims 8 and 9 of the '208 patent as compared to instant claim 89. The difference is further amplified by the definition of the C7 substituent as β-R_{7a}COO- (rather than α- or β-R_{7a}COO-) and consideration of differences in the C7 substituent as discussed herein above. Thus, as above for claim 1, claim 89 is patentable in view of the '208 patent claims.

Further, as described above for Group 1, the mechanistic dissection and recombination of components of the compounds is not allowed. In this case, the only way that the compounds of instant claim 89 could be derived from the compounds of claims 8 and 9 of the '208 patent is through such impermissible dissection and recombination.

Claims 90-95 incorporate all the elements of claim 89 and further define substituents of the taxane compounds. Claims 166-167 are directed to methods of inhibiting tumor growth through oral administration of pharmaceutical compositions containing the taxane compounds of claim 89. Claims 168-169 are directed to pharmaceutical compositions of the compounds of claim 89. Thus, the claims of Group V are patentable over the '208 patent for the same reasons as claim 89.

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[21] In re Petering, 133 U.S.P.Q. 275, 280 (C.C.P.A. 1962).

In summary, the Office has failed to identify any suggestion or motivation that would have led a person of ordinary skill from the compounds defined by the claims of the '208 patent to the compounds defined by the Group V claims. Accordingly, a *prima facie* case of obviousness has not been established with respect to the Group V claims.

6. The Group VI Claims (Claims 102-108 and 115-117)

Claim 102 is representative of the Group VI claims. It is dependent upon claim 89 and is patentable for the same reasons as those stated with respect to claim 89. It is separately and independently patentable over the claims of the '208 patent for the following reasons.

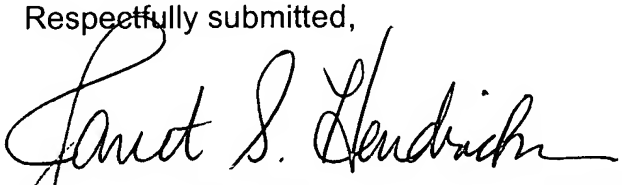
Claim 102 further requires a propionyloxy or butyryloxy group at the C7 position. The compounds defined by claim 102 have multiply different combinations of taxane substituents (as detailed in Table 2) and a propionyloxy or butyryloxy group at the C7 position; the compounds of the '208 patent claims have an acyloxy group at the C7 position. Claims 8 and 9 would not have suggested the selection of a propionyloxy or butyryloxy group at the C7 position and actually would have led a skilled artisan away from the defined combination of claim 102 and to the selection of a hydrogen at the C7 position. Accordingly, a *prima facie* case of obviousness has not been established with respect to the Group V claims.

C. Conclusion

For the foregoing reasons, appellants respectfully submit claims 1-85, 89-95, 102-108, 115-117, 122-132, 134-137, 140-146, 148-150, 153-159, 161-163 and 166-169 are patentable over Holton et al., U.S. Patent No. 6,462,208, and request that the rejection of these claims as being unpatentable under the judicially created doctrine of obviousness-type double patenting be reversed.

A check in the amount of $950.00 is enclosed ($450.00 for a two month extension of time; $500.00 for the Appeal Brief filing fee). The Commissioner is hereby authorized to charge any additional fees which may be required to Deposit Account No. 19-1345.

Respectfully submitted,



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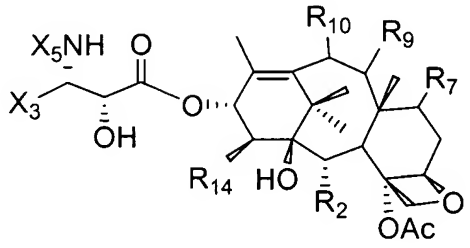
APPENDIX

What is claimed is:

1. (previously amended): A taxane having the formula



wherein

R_2 is acyloxy;

R_7 is $R_{7a}COO$-;

R_{7a} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo wherein said hydrocarbyl or substituted hydrocarbyl contains carbon atoms in the alpha and beta positions relative to the carbon atom of which R_{7a} is a substituent and wherein said substituted hydrocarbyl is substituted with a group selected from halogen, heterocyclo, alkoxy, alkenoxy, alkynoxy, aryloxy, hydroxy, protected hydroxy, acyloxy, nitro, cyano, thiol, ketals, acetals and ethers;

R_9 is keto, hydroxy, or acyloxy;

R_{10} is hydroxy;

R_{14} is hydrido or hydroxy;

X_3 is heterocyclo;

X_5 is $-COX_{10}$, and X_{10} is alkyl, alkenyl, alkynyl or heterocyclo; or

X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, alkenyl, alkynyl or heterocyclo; and

Ac is acetyl.

2. (Original): The taxane of claim 1 wherein R_{7a} is substituted or unsubstituted C_2 - C_8 alkyl, C_2 - C_8 alkenyl or C_2 - C_8 alkynyl.

3. (Previously amended): The taxane of claim 2 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

4. (Previously amended): The taxane of claim 2 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

5. (Previously Amended): The taxane of claim 2 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

6. (Original): The taxane of claim 2 wherein R_{14} is hydrido.

7. (Previously amended): The taxane of claim 6 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

8. (Previously amended): The taxane of claim 6 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

9. (Previously amended): The taxane of claim 6 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

10. (Original): The taxane of claim 2 wherein R_2 is benzoyloxy.

11. (Previously amended): The taxane of claim 10 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

12. (Previously amended): The taxane of claim 10 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

13. (Previously amended): The taxane of claim 10 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

14. (Original): The taxane of claim 2 wherein R_{14} is hydrido and R_9 is keto.

15. (Previously amended): The taxane of claim 14 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

16. (Previously amended): The taxane of claim 14 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

17. (Previously amended): The taxane of claim 14 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

18. (Original): The taxane of claim 2 wherein R_2 is benzoyloxy and R_9 is keto.

19. (Previously amended): The taxane of claim 18 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

20. (Previously amended): The taxane of claim 18 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

21. (Previously amended): The taxane of claim 18 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

22. (Original): The taxane of claim 2 wherein R_{14} is hydrido and R_2 is benzoyloxy.

23. (Previously amended): The taxane of claim 22 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

24. (Previously amended): The taxane of claim 22 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

25. (Previously amended): The taxane of claim 22 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

26. (Original): The taxane of claim 2 wherein R_{14} is hydrido, R_9 is keto, and R_2 is benzoyloxy.

27. (Previously amended): The taxane of claim 26 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

28. (Previously amended): The taxane of claim 26 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

29. (Previously amended): The taxane of claim 26 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

30. (Original): The taxane of claim 1 wherein R_{7a} is C_2 - C_8 alkyl.

31. (Previously amended): The taxane of claim 30 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

32. (Previously amended): The taxane of claim 30 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-

butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

33. (Previously amended): The taxane of claim 30 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

34. (Original): The taxane of claim 30 wherein R_{14} is hydrido.

35. (Previously amended): The taxane of claim 34 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

36. (Previously amended): The taxane of claim 34 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

37. (Previously amended): The taxane of claim 34 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

38. (Original): The taxane of claim 30 wherein R_2 is benzoyloxy.

39. (Previously amended): The taxane of claim 38 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

40. (Previously amended): The taxane of claim 38 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-

butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

41. (Previously amended): The taxane of claim 38 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

42. (Original): The taxane of claim 30 wherein R_{14} is hydrido and R_9 is keto.

43. (Previously amended): The taxane of claim 42 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

44. (Previously amended): The taxane of claim 42 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

45. (Previously amended): The taxane of claim 42 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

46. (Original): The taxane of claim 30 wherein R_2 is benzoyloxy and R_9 is keto.

47. (Previously amended): The taxane of claim 46 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

48. (Previously amended): The taxane of claim 46 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-

butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

49. (Previously amended): The taxane of claim 46 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

50. (Original): The taxane of claim 30 wherein R_{14} is hydrido and R_2 is benzoyloxy.

51. (Previously amended): The taxane of claim 50 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

52. (Previously amended): The taxane of claim 50 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

53. (Previously amended): The taxane of claim 50 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

54. (Original): The taxane of claim 30 wherein R_{14} is hydrido, R_9 is keto, and R_2 is benzoyloxy.

55. (Previously amended): The taxane of claim 54 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

56. (Previously amended): The taxane of claim 54 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-

pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

57. (Previously amended): The taxane of claim 54 wherein X_5 is -COX_{10} and X_{10} is iso-butenyl, or X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

58. (Original): The taxane of claim 1 wherein R_{7a} is ethyl.

59. (Previously amended): The taxane of claim 58 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

60. (Previously amended): The taxane of claim 58 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

61. (Previously amended): The taxane of claim 58 wherein X_5 is -COX_{10} and X_{10} is iso-butenyl, or X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

62. (Original): The taxane of claim 58 wherein R_{14} is hydrido.

63. (Previously amended): The taxane of claim 62 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

64. (Previously amended): The taxane of claim 62 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-

pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

65. (Previously amended): The taxane of claim 62 wherein X_5 is -COX_{10} and X_{10} is iso-butenyl, or X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

66. (Original): The taxane of claim 58 wherein R_2 is benzoyloxy.

67. (Previously amended): The taxane of claim 66 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

68. (Previously amended): The taxane of claim 66 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is -$COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

69. (Previously amended): The taxane of claim 66 wherein X_5 is -COX_{10} and X_{10} is iso-butenyl, or X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

70. (Original): The taxane of claim 58 wherein R_{14} is hydrido and R_9 is keto.

71. (Previously amended): The taxane of claim 70 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

72. (Previously amended): The taxane of claim 70 wherein X_5 is -COX_{10} and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-

pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

73. (Previously amended): The taxane of claim 70 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

74. (Original): The taxane of claim 58 wherein R_2 is benzoyloxy and R_9 is keto.

75. (Previously amended): The taxane of claim 74 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

76. (Previously amended): The taxane of claim 74 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

77. (Previously amended): The taxane of claim 74 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

78. (Original): The taxane of claim 58 wherein R_{14} is hydrido and R_2 is benzoyloxy.

79. (Previously amended): The taxane of claim 78 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

80. (Previously amended): The taxane of claim 78 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

81. (Previously amended): The taxane of claim 78 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

82. (Original): The taxane of claim 58 wherein R_{14} is hydrido, R_9 is keto, and R_2 is benzoyloxy.

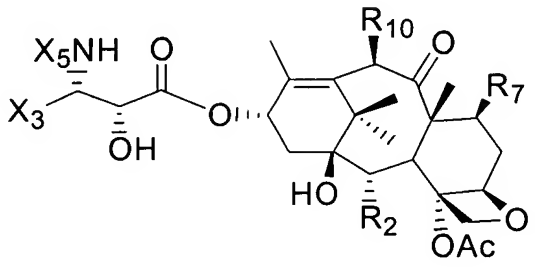
83. (Previously amended): The taxane of claim 82 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

84. (Previously amended): The taxane of claim 82 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

85. (Previously amended): The taxane of claim 82 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

86. - 88. (Canceled).

89. (previously amended): A taxane having the formula



R_2 is benzoyloxy;

R_7 is $R_{7a}COO$-;

R_{10} is hydroxy;

X_3 is heterocyclo;

X_5 is $-COX_{10}$, and X_{10} is alkyl, alkenyl, alkynyl or heterocyclo; or

X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, alkenyl, alkynyl or heterocyclo; and

R_{7a} is hydrocarbyl, substituted hydrocarbyl, or heterocyclo wherein said hydrocarbyl or substituted hydrocarbyl contains carbon atoms in the alpha and beta positions relative to the carbon of which R_{7a} is a substituent and wherein said substituted hydrocarbyl is substituted with a group selected from halogen, heterocyclo, alkoxy, alkenoxy, alkynoxy, aryloxy, hydroxy, protected hydroxy, acyloxy, nitro, cyano, thiol, ketals, acetals and ethers; and

Ac is acetyl.

90. (Previously amended): The taxane of claim 89 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

91. (Previously amended): The taxane of claim 90 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is

substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

92. (Previously amended): The taxane of claim 90 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

93. (Original): The taxane of claim 89 wherein X_3 is furyl or thienyl.

94. (Previously amended): The taxane of claim 93 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

95. (Previously amended): The taxane of claim 93 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

96. - 101. (Canceled).

102. (Original): The taxane of claim 89 wherein R_{7a} is ethyl or propyl.

103. (Previously amended): The taxane of claim 102 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

104. (Previously amended): The taxane of claim 103 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-

butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

105. (Previously amended): The taxane of claim 103 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

106. (Original): The taxane of claim 102 wherein X_3 is furyl or thienyl.

107. (Previously amended): The taxane of claim 106 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

108. (Previously amended): The taxane of claim 106 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

109. - 114. (Canceled).

115. (Previously amended): The taxane of claim 89 wherein X_3 is furyl or thienyl, R_{7a} is ethyl, and X_5 is $-COX_{10}$ and X_{10} is iso-butenyl.

116. (Previously amended): The taxane of claim 89 wherein X_3 is substituted furyl, R_{7a} is ethyl, and X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

117. (Previously amended): The taxane of claim 89 wherein X_3 is substituted thienyl, R_{7a} is ethyl, and X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

118. - 121. (Canceled).

122. (Original): A pharmaceutical composition comprising the taxane of claim 1 and at least one pharmaceutically acceptable carrier.

123. (Previously amended): The pharmaceutical composition of claim 122 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

124. (Previously amended): The pharmaceutical composition of claim 123 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

125. (Previously amended): The pharmaceutical composition of claim 123 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

126. (Original): The pharmaceutical composition of claim 122 wherein R_{7a} is ethyl or propyl.

127. (Previously amended): The pharmaceutical composition of claim 126 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

128. (Previously amended): The pharmaceutical composition of claim 127 wherein X_5 is $-COX_{10}$ and X_{10} is substituted or unsubstituted 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl, or X_5 is $-COOX_{10}$ and X_{10} is substituted or unsubstituted methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, cyclobutyl, n-pentyl, iso-pentyl, tert-pentyl, sec-

pentyl, cyclopentyl, n-hexyl, iso-hexyl, sec-hexyl, tert-hexyl, cyclohexyl, C_2 - C_8 alkenyl, or C_2 - C_8 alkynyl.

129. (Previously amended): The pharmaceutical composition of claim 127 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

130. (Previously amended): The pharmaceutical composition of claim 123 wherein X_3 is furyl or thienyl, R_{7a} is ethyl, and X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

131. (Previously amended): The pharmaceutical composition of claim 123 wherein X_3 is substituted or unsubstituted furyl, R_{7a} is ethyl, and X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

132. (Previously amended): The pharmaceutical composition of claim 123 wherein X_3 is substituted or unsubstituted thienyl, R_{7a} is ethyl, and X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

133. - 134. (Canceled).

135. (Previously amended): The pharmaceutical composition of claim 123 wherein X_3 is 2-furyl or 2-thienyl, R_{7a} is ethyl, X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

136. (Previously amended): The pharmaceutical composition of claim 123 wherein X_3 is 2-furyl, R_{7a} is ethyl, X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

137. (Previously amended): The pharmaceutical composition of claim 123 wherein X_3 is 2-thienyl, R_{7a} is ethyl, X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

138. - 139. (Canceled).

140. (Original): A composition for oral administration comprising the taxane of claim 1 and at least one pharmaceutically acceptable carrier.

141. (Previously amended): The composition of claim 140 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

142. (Previously amended): The composition of claim 140 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

143. (Original): The composition of claim 140 wherein R_{7a} is ethyl or propyl.

144. (Previously amended): The composition of claim 143 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

145. (Previously amended): The composition of claim 144 wherein X_5 is $-COX_{10}$ and X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

146. (Previously amended): The composition of claim 144 wherein X_3 is furyl, or thienyl, R_{7a} is ethyl, and X_5 is $-COX_{10}$ wherein X_{10} is iso-butenyl, or X_5 is $-COOX_{10}$ and X_{10} is iso-propyl.

147. (Canceled).

148. (Previously amended): The composition of claim 146 wherein X_3 is 2-furyl or 2-thienyl, R_{7a} is ethyl, X_5 is $-COOX_{10}$ and X_{10} is iso-propyl or X_5 is $-COX_{10}$ and X_{10} is iso-butenyl.

149. (Previously amended): The composition of claim 148 wherein X_3 is 2-furyl, R_{7a} is ethyl, X_5 is $-COX_{10}$ and X_{10} is iso-butenyl.

150. (Previously amended): The composition of claim 148 wherein X_3 is 2-thienyl, R_{7a} is ethyl, X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

151. - 152. (Canceled).

153. (Original): A method of inhibiting tumor growth in a mammal, said method comprising orally administering a therapeutically effective amount of a pharmaceutical composition containing the taxane of claim 1 and at least one pharmaceutically acceptable carrier.

154. (Previously amended): The method of claim 153 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

155. (Previously amended): The method of claim 154 wherein X_5 is -COX_{10} and X_{10} is iso-butenyl, or X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

156. (Original): The method of claim 153 wherein R_{7a} is ethyl or propyl.

157. (Previously amended): The method of claim 156 wherein X_3 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl.

158. (Previously amended): The method of claim 157 wherein X_5 is -COX_{10} and X_{10} is iso-butenyl, or X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

159. (Previously amended): The method of claim 153 wherein X_3 is furyl or thienyl, R_{7a} is ethyl, and X_5 is -COX_{10} and X_{10} is iso-butenyl, or X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

160. (Canceled).

161. (Previously amended): The method of claim 159 wherein X_3 is 2-furyl or 2-thienyl, R_{7a} is ethyl, X_5 is -$COOX_{10}$ and X_{10} is iso-propyl or X_5 is -COX_{10} and X_{10} is iso-butenyl.

162. (Previously amended): The method of claim 161 wherein X_3 is 2-furyl, R_{7a} is ethyl, X_5 is -COX_{10} and X_{10} is iso-butenyl.

163. (Previously amended): The method of claim 159 wherein X_3 is 2-thienyl, R_{7a} is ethyl, X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

164. - 165. (Canceled).

166. (Original): A method of inhibiting tumor growth in a mammal, said method comprising orally administering a therapeutically effective amount of a pharmaceutical composition containing the taxane of claim 89 and at least one pharmaceutically acceptable carrier.

167. (Previously amended): The method of claim 166 wherein X_3 is furyl or thienyl, R_{7a} is ethyl, X_5 is -COX_{10} and X_{10} is iso-butenyl, or X_5 is -$COOX_{10}$ and X_{10} is iso-propyl.

168. (Original): A pharmaceutical composition comprising the taxane of claim 89 and at least one pharmaceutically acceptable carrier.

169. (Original): A pharmaceutical composition comprising the taxane of claim 93 and at least one pharmaceutically acceptable carrier.